REMARKS

Upon entry of these amendments, claims 1, 15-20, 26-27, 31-50, 53-56, 63, 68-125 will be pending in this application. Claims 1, 15-18, 26-27, 31-38, 53, 68-75, 77-78, 81, 84-125 are under examination. Claims 19-20, 39-50, 54-56, 63, 76, 79-80 and 82-83 have been withdrawn as directed to non-elected subject matter. Claims 2-14, 21-25, 28-30, 51-52, 57-62 and 64-67 have previously been cancelled, without prejudice or disclaimer. Applicants have herein amended claim 1 and 81 and have added new claims 84-125. Support for the amendments to claims 1 and 81 can be found at least at page 7, lines 17-19 and at page 19, lines 3-10 of the specification. Support for new claim 84 can be found at least at page 7, lines 16-17 and at page 8, line 5 of the specification; support for new claim 85 can be found at least at page 7, lines 22-26 of the specification; support for new claim 86 can be found at least at page 7, lines 17-19 of the specification; support for new claim 87 can be found at least at page 7, lines 26-29 of the specification; support for new claim 88 can be found at least at page 7, lines 16-17 and at page 8, line 5 of the specification; support for new claim 89 can be found at least at page 7, lines 22-26 of the specification; support for new claim 90 can be found at least at page 7, lines 17-19 of the specification; support for new claim 91 can be found at least at page 7, lines 26-29; and support for new claims 92-125 can at least be found in claims 1, 15-18, 26-38, 53, 68-75, 77-78, and 84-91, respectively, as originally filed.

Accordingly, no new matter has been added herein.

Claim Rejections--35 U.S.C.§ 102(b)

Claims 1, 15-18, 26, 31, 32, 53, and 81 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 1 136 557 A1 ("Schilfgaarde"). According to the Examiner, Schilfgaarde teaches the use of recombinant techniques to obtain paracytin peptides fused to other therapeutically active peptides and proteins. (*See* Office Action at page 5). Applicants traverse.

Claims 1 and 81 have been amended herein to include the limitation "wherein, when the effector is a polypeptide, the penetrating module is encoded by a chimeric gene sequence." Schilfgaarde does not teach or suggest such a chimeric penetrating module as is recited in the amended claims. Because Schilfgaarde fails to teach or suggest all the limitations of claims 1 and 81, as amended herein, Applicants submit that these claims are not anticipated by Schilfgaarde. Therefore, Applicants request that this rejection be withdrawn.

Likewise, claims 15-18, 26, 31-32 and 53 each depend (directly or indirectly) on claim 1, as amended herein. As such, they necessarily contain all of the limitations of this amended claim. Therefore, for all of the reasons articulated above, Applicants submit that these claims are likewise not anticipated by Schilfgaarde.

Moreover, new claims 84-91 also depend (directly or indirectly) from claim 1, as amended herein. Additionally, new claim 92 recites the same limitation that was added to amended claim 1, and new claims 93-125 depend (directly or indirectly) on new claim 92. Thus, for the reasons articulated above, Applicants believe that this rejection also does not apply to the new claims presented herein.

Claim Rejections--35 U.S.C.§ 103

Claims 1, 15-18, 26, 27, 31-38, 53, 68-75, 77, 78 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1 136 557 A1 ("Schilfgaarde") in view of Juliano, et al., Current Opinion in Molecular Therapeutics, 2000, 2, 297-303 ("Juliano") further in view of Lindgren, et al., TIPS, 2000, 21, 99-103 ("Lindgren") and further in view of U.S. Patent No. 5,286,637 ("Veronese"). According to the Examiner, the suggestion to combine these references stems from the fact that the primary reference, Schilfgaarde, teaches the use of recombinant techniques to obtain paracytin peptides that are conjugated to other active peptides or proteins. (*See* Office Action at page 8). Therefore, the Examiner concludes that paracytin peptides, when conjugated to other active peptides or proteins, meet the limitations of the claimed invention. (*See* Office Action page 8). Moreover, the Examiner further states that Lindgren teaches the conjugation of biomolecules such as peptides, proteins, nucleic acids to cell penetrating peptides and further suggests that drugs and other research tools (*e.g.*, diagnostic) agents can be synthesized for cellular delivery. (*See* Office Action page 8). Therefore, for those reasons (as well as for those reasons articulated in the February 7, 2006 and May 26, 2006 Office Actions), the Examiner concludes that these claims are obvious in view of the cited references. Applicants traverse.

For at least the reasons articulated above, Applicants contend that Schilfgaarde does not teach or suggest the penetrating modules recited in the amended claims. Specifically, Schilfgaarde does not teach or suggest a penetrating module wherein, when the effector is a polypeptide the penetrating module is encoded by a chimeric gene sequence. The addition of

Juliano and/or Lindgren does not cure these deficiencies. Both Juliano and Lindgren teach the use of cell penetrating peptides conjugated to biologically active peptides or proteins. However, neither Juliano nor Lindgren teaches or suggests a penetrating module comprising a penetrating peptide and an effector, wherein, when the effector is a polypeptide, the penetrating module is encoded by a chimeric gene sequence. Moreover, the addition of Veronese likewise does not supply the teaching or suggestion missing from these other references, as Veronese teaches the pegylation of biologically active peptides or proteins for advantageous pharmacokinetics. However, there is no teaching or suggestion in Veronese of a penetrating module comprising a penetrating peptide and an effector, wherein, when the effector is a polypeptide, the penetrating module is encoded by a chimeric gene sequence.

Therefore, because the combination of Schilfgaarde, Juliano, Lindgren, and/or Veronese fails to teach or suggest each of the limitations of the pending claims, as amended herein, Applicants submit that the Examiner has failed to set forth a proper *prima facie* case of obviousness. Thus, Applicants request that this rejection of claims 1 and 81 be withdrawn.

Claims 15-18, 26-27, 31-38, 53, 68-75, 77-78 and new claims 84-91 each depend (directly or indirectly) on claim 1, as amended herein. Therefore, they necessarily contain all of the limitations of that claim. Additionally new claim 92 recites the same limitation added in amended claim 1. Moreover, because new claims 93-125 each directly or indirectly depend from new claim 92 they necessarily contain all of the limitations of that claim. Thus, Applicants submit that these claims are likewise not obvious over Schilfgaarde, Juliano, Lindgren, and/or Veronese, for the reasons set forth above.

Thus, for all of these reasons, Applicants request that the rejection of claims 1, 15-18, 26-27, 31-38, 53, 68-75, 77-78 and 81 be withdrawn.

Claim Rejections--Double Patenting

The Examiner has maintained the rejection of claims 1, 31, 33-34 and 53 for obviousness-type double patenting over claims 1, 2, 90, 97, 101 and 102 of U.S. Application No. 10/665,184, which correspond to claims 1, 2, 31, 32 and 34 of U.S. Patent No. 7,115,707 ("the '707 patent"). The Examiner has previously indicated that the subject matter claimed in the instant application is fully disclosed in the referenced copending application, U.S. Application No. 10/665,184, now U.S. Patent No. 7,115,707 ("the '707 patent") and would be covered by any patent granted on that copending application since the referenced copending

application and the instant application are claiming common subject matter. (*See* May 26, 2006 Office Action at page 6). Specifically, in that Office Action, the Examiner stated that "The claims are drawn to penetrating peptides and pharmaceutical compositions comprising the penetrating peptide and effector modules." (*See* May 26, 2006 Office Action at page 6). Applicants disagree.

Claim 1 has been amended herein to recite a penetrating module comprising an effector coupled or fused to a penetrating peptide consisting of at least one amino acid sequence selected from the group consisting of SEQ ID NOS:1-15, SEQ ID NOS:25-29, and at least 12 contiguous amino acids of any of these peptides. Moreover, as noted above, claim 1 has also been amended to include the limitation "wherein, when the effector is a polypeptide, the penetrating module is encoded by a chimeric gene sequence." The '707 patent does not claim such a penetrating module. As such, Applicants submit that the rejection of claim 1 for obvious-type double patent in view of the '707 patent has been overcome..

Likewise, claims 31, 33-34 and 53 each depend (directly or indirectly) on amended claim 1. As such, they necessarily contain all the limitations of amended claim 1. Therefore, for all the reasons articulated above, Applicants submit that this rejection of these claims has also been overcome.

Moreover, new claim 92 recites a penetrating module consisting of an effector coupled or fused to a penetrating peptide consisting of at least one amino acid sequence selected from the group consisting of SEQ ID:24 and at least 12 contiguous amino acids of SEQ ID NO:24, wherein, when the effector is a polypeptide, the module is encoded by a chimeric gene sequence. Such a penetrating module is not claimed in the '707 patent. Thus, Applicants submit that this rejection for obviousness-type double patenting does not apply to new claim 92 (or to dependent claims 93-125).

Therefore, Applicants submit that this obviousness-type double patenting rejection has been overcome and should be withdrawn.

CONCLUSION

Applicant submits that this paper is fully responsive and that the application is in condition for allowance. Such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below. The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 24348-501 NATL.

Respectfully submitted,

Dated: April 30, 2007

Ivor R. Elrifi, Reg. No. 39,529
Christina K. Stock, Reg. No. 45,899
Attorneys for Applicants
MINTZ LEVIN COHN FERRIS
GLOVSKY and POPEO PC
Tel.: (617) 542-6000
Fax: (617) 542-2241
Customer No.: 30623